

Lobular Carcinoma in Situ With Microinvasion

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Six patients with lobular carcinoma in situ with microinvasion were described in this report. Lobular carcinoma in situ is not known to progress to microinvasive disease. Although this feature is rare, the current understanding that lobular carcinoma in situ is a marker needs to be revised.

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INTRODUCTION

In the original report by Foote and Stewart [1], lobular carcinoma in situ (LCIS) was described as a rare form of mammary cancer. Further observations and experience with the nonmalignant behavior of LCIS led to the revision of its designation as a marker of high risk. This concept of risk marker rather than actual cancer has led to the current recommendation for its surgical treatment or, more aptly, nontreatment.

LCIS as a high-risk marker, confers an equal risk in both breasts. If a malignancy develops, it is more often ductal carcinoma, rather than lobular. Development of such tumors is not limited to the area of lobular carcinoma in situ, but rather random in location [2-4]. Since LCIS is neither a "precursor" nor "preinvasive," the current prevailing view is that it does not progress to "microinvasive" or invasive lobular carcinoma. In our experience as well as that of others, rare cases of lobular carcinoma in situ with microinvasion were noted or reported [5,6]. In this report we describe six cases of LCIS encountered between January 1996 and December 1996 bearing the feature of microinvasion.

MATERIALS AND METHODS

Six patients with LCIS with microinvasion are described. Photomicrographs of four lesions accompany this report.

Case 1

This 60-year-old patient previously underwent a left mastectomy in 1989 for infiltrating ductal carcinoma. A

minimal right outer upper quadrant thickening was noted in 1995. A mammogram showed a loose cluster of small microcalcifications.

Pathology. Multifocal LCIS was found, some arising in sclerosing adenosis. The LCIS was essentially of small cell type composed of loosely cohesive small cells with uniform nuclei. One focus showed stromal microinvasion in the form of single tumor cells or small groups of tumor cells in fibrous stroma (Fig. 1). In addition, florid sclerosing adenosis, microglandular adenosis, and atypical lobular hyperplasia were noted.

Treatment. A right modified mastectomy was performed. In the specimen, atypical lobular hyperplasia was found but no lobular carcinoma in situ. Twenty-two nodes were all negative.

Case 2

The physician detected a 1.5 cm left upper central mass in this 46-year-old patient. The mammogram was negative.

Pathology. Practically all lobules in all the sections were involved either by LCIS of small cell type or by atypical lobular hyperplasia with ductal extension. There were two separate foci of microinvasive lobular carcinomas, each measuring less than 2 mm, composed of short Indian file cords and small nests of small tumor cells (Fig. 2). Both foci were adjacent to a duct involved by LCIS.

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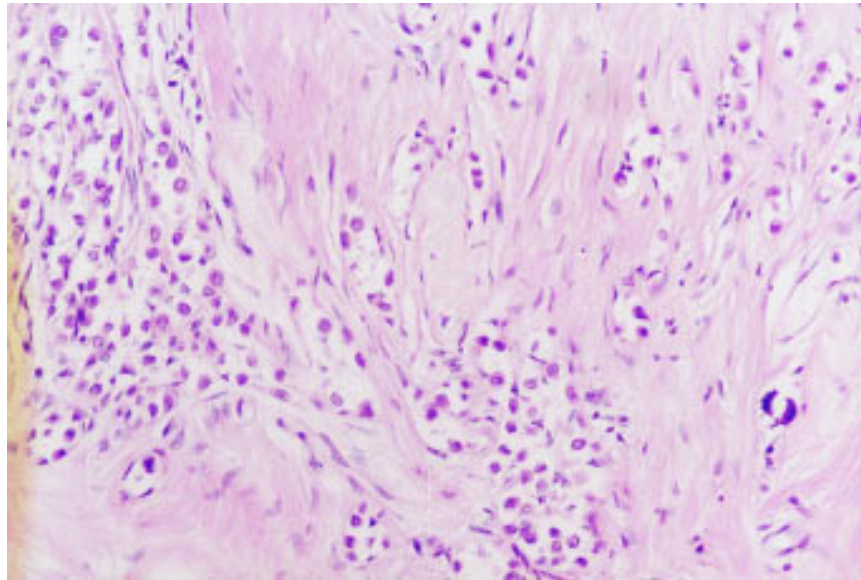


Fig. 1. Case 1. Lobular carcinoma in situ arising in sclerosing adenosis with stromal microinvasion composed of scattered single to few short cords of loosely cohesive small tumor cells in stroma.

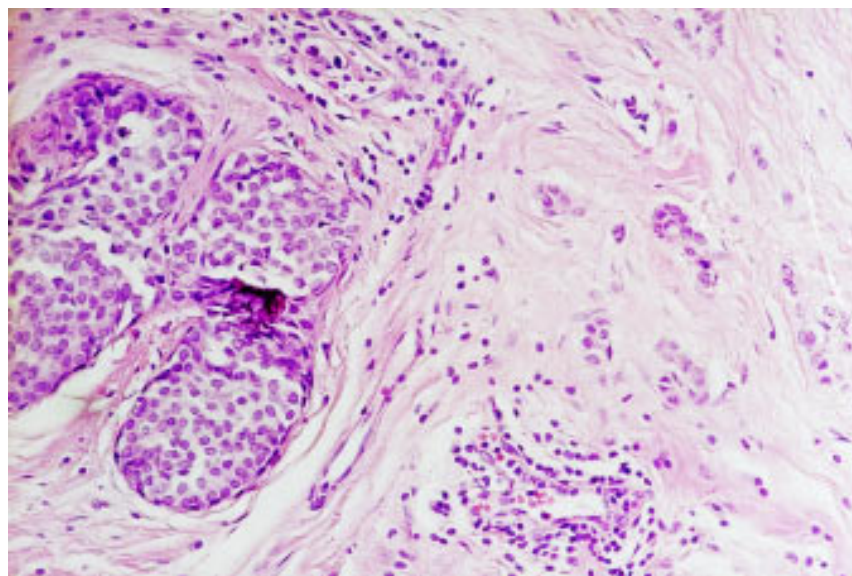


Fig. 2. Case 2. On the left field is LCIS, small cell type with microinvasive lobular carcinoma on the right field composed of identical small tumor cells forming small nests and cords. The tumor cells are only slightly larger than the lymphocytes around a vessel.

Treatment. The biopsy completely excised the invasive lesions. An axillary dissection showed 14 negative nodes. No radiation was given to the breast.

Case 3

Mammographic microcalcifications and a mammographic mass nearby were noted in this 84-year-old patient. Clinically, a mass was not palpable.

Pathology. The sections showed involutional changes with only occasional lobules containing LCIS of

large cell type, composed of large cuboidal cells with clear to eosinophilic, almost apocrine type, cells with relatively large nuclei and nucleoli. Most of the remaining ducts showed Pagetoid involvement by LCIS. Two separate foci of microinvasive lobular carcinoma surrounded involved ducts (Fig. 3).

Treatment. A lumpectomy of the biopsy area demonstrated atypical lobular hyperplasia and a few ducts with Pagetoid spread of lobular carcinoma but no invasive tumor. Lumpectomy was performed without radiation.

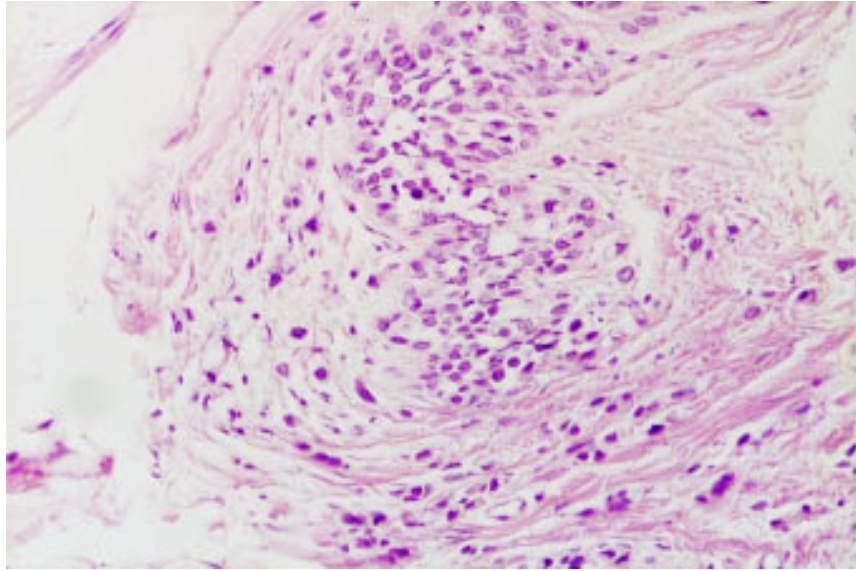


Fig. 3. Case 3. On the midfield is a duct replaced by neoplastic lobular cells. Around it is microinvasive lobular carcinoma. Note blurring of the ductal basement membrane. Elsewhere are lobules with typical LCIS.

Case 4

This 41-year-old patient underwent a left mastectomy for a mammographically detected infiltrating lobular carcinoma of 9 mm. and all 14 nodes were negative. A prophylactic right total mastectomy was done at the same time. Her right mammogram was negative and a palpable mass was not present.

Pathology. In the “prophylactically” resected right breast was extensive LCIS, of small cell type with ductal extension. There were four foci of infiltrating lobular carcinomas, three measuring 1–2 mm. and one measuring 5 mm. The three microinvasive foci were adjacent to or surrounding an involved duct (Fig. 4).

Treatment. A right axillary dissection was performed. Sixteen nodes were negative.

Case 5

Two clusters of microcalcifications of the right upper outer quadrant were detected on mammogram in this 46-year-old patient.

Pathology. Two separate biopsies were taken from the right breast with practically all sections showing extensive LCIS predominantly of small cell type. Only rare lobules showed large cell type LCIS. In one biopsy, a 4-mm tubulolobular variant infiltrating lobular carcinoma was seen. In the second fragment, a microinvasive lobular carcinoma was found around a duct involved by lobular neoplasia although no LCIS was seen in the immediate vicinity.

Treatment. The patient underwent a right modified mastectomy. There were foci of atypical lobular hyperplasia and seven nodes were negative. A left breast bi-

opsy revealed focal atypical ductal hyperplasia and atypical lobular hyperplasia.

Case 6

A stage III carcinoma of the right breast in this 45-year-old patient was treated with chemotherapy and mastectomy. Left breast masses were palpable. The mammogram showed irregular densities. The patient elected mastectomy.

Pathology. The left mastectomy specimen was described as “lumpy,” although no discrete tumor was noted. Histologically there were extensive multiple foci of LCIS, of both small and large cell types, with ductal extension. There were two separate foci of microinvasive lobular carcinoma each measuring 1 mm. In one focus, the microinvasive carcinoma was around an involved duct in the absence of LCIS in its immediate vicinity, while in the other, it was adjacent to LCIS without an involved duct (Fig. 5A,B). All nine nodes were negative.

RESULTS

In three of six patients, there was a clinical mass or thickening that prompted biopsy. Subtle microcalcifications and/or densities were noted on mammograms in four of six patients. In one patient there was no clinical or mammographic change noted. The extent of LCIS was extensive in five of six patients. The size of the microinvasive lobular carcinoma was less than 2 mm in all patients. In one patient microinvasive changes were noted in three areas; in three patients, two areas; and in one patient, one area. In two patients, in addition to microinvasive lobular carcinoma, there was additional invasive lobular carcinoma of 4 mm and 5 mm.

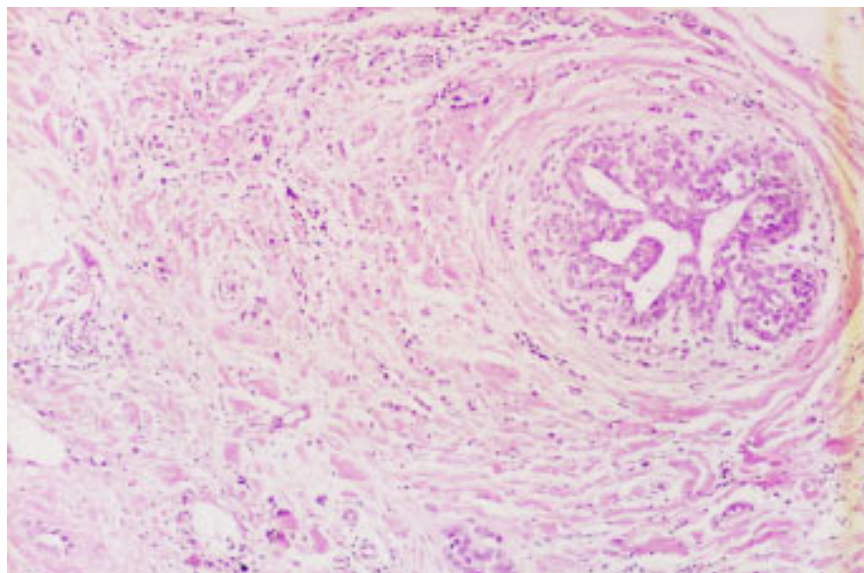


Fig. 4. Case 4. Duct showing Pagetoid involvement by lobular neoplasia around which is microinvasive lobular carcinoma composed of cords of small uniform tumor cells. Elsewhere are lobules with LCIS.

Descriptions of Pathologic Findings

None of the lesions in the biopsies (Cases 1, 2, 3, and 5) and mastectomies (Cases 4 and 6) was recognized grossly. Biopsy specimens were serially sectioned at 4-mm intervals and entirely embedded. From the mastectomy specimens, five sections from each quadrant as well as nipple and subareolar regions were taken.

In five of the six cases, LCIS was extensive, involving most of the lobules in most or all of the sections. The number of sections or slides ranged from 12 to 30. In Case 3, with involutional changes, only occasional lobules were left that showed LCIS, of large cell type. Most of the remaining ducts however, were involved by lobular neoplasia. Three cases of LCIS were exclusively small cell types and one mostly large cell type. One to three separate foci of microinvasive (<2-mm) carcinoma were found in two patients. It is interesting to note that ductal involvement by lobular neoplasia was present in all the cases. Except for one focus, all the foci of microinvasion were adjacent to or were surrounding such an involved duct. It is possible that once the LCIS involves ducts, it becomes a "precursor" to invasion, much like ductal carcinoma in situ (DCIS), in addition to being a "marker" lesion.

DISCUSSION

The distinction between DCIS and LCIS is that the former is known to progress to invasive disease while the latter is not. DCIS is considered pre-invasive, while LCIS is thought to be the marker of increased risk of subsequent development of invasive carcinoma.

Since DCIS with microinvasion is seen relatively fre-

quently, its pre-invasive role is readily acceptable. A lack of such observation in LCIS so far supported its assignment as a high-risk marker.

The six patients described in this report were diagnosed with LCIS with microinvasion. Such observations have been few [5–8] and sometimes reported in passing. Coyne et al. [5] reported a patient with LCIS with microinvasion found in a hamartoma. In a report on duct carcinoma in situ with microinvasion, Wong et al. [6] briefly described a patient with LCIS with microinvasion. This entity has been referred to in a report on non-palpable breast cancers (G. LeBouedec, J. Daulat, personal communication, 1996). Of these 12 cases with in situ breast cancer with microinvasion, five had LCIS with microinvasion and seven had DCIS with microinvasion [7]. Our six patients with LCIS and microinvasion represent one-third of the total number of our patients diagnosed with LCIS over a 1-year period. During the same period, more than 400 patients with primary breast cancers, invasive and noninvasive, were treated.

Since LCIS is encountered relatively infrequently, and LCIS with microinvasion much less frequently reported, clinical significance of this entity is limited. It is noteworthy that some of the LCIS appear to present with, or to progress to, microinvasive lobular carcinoma. The two patients with an additional 4-mm and 5-mm invasive lobular carcinoma suggest a chain of progressive events.

Most often, the diagnosis of LCIS is incidental to benign lesions found by biopsy. In five of these six patients, there was either a clinical mass or microcalcifications that prompted biopsy. The presence of such clinical or mammographic changes may indicate an increased likelihood of microinvasive transition.

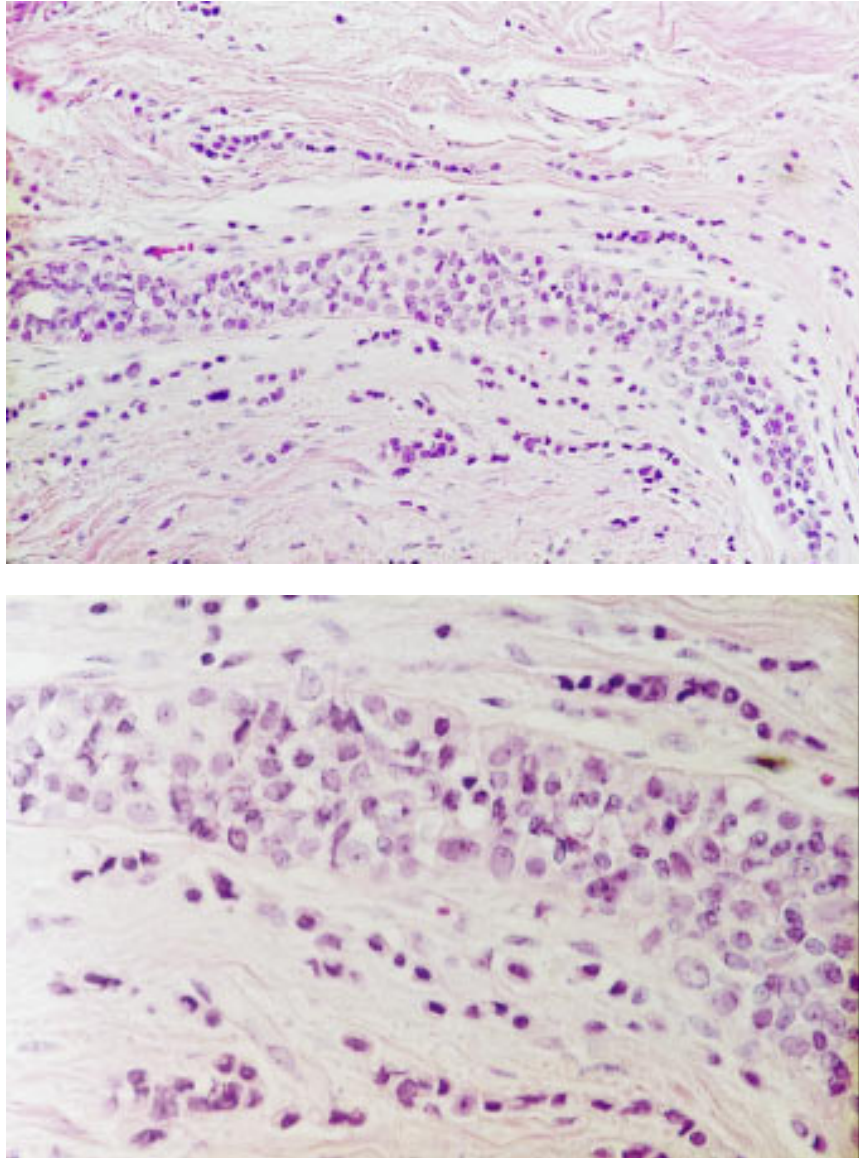


Fig. 5. Case 6. **A:** Low-power view of duct involved by lobular neoplasia. Around it are Indian-file cords of microinvasive lobular carcinoma. Elsewhere there is extensive LCIS of both small and large cell types. **B:** High-power view showing involved duct replaced by a mixture of small and large neoplastic cells. Note one cell apparently traversing the basement membrane of the involved duct.

In Oetteson's series, recurrences were found more frequently among LCIS with large cells [8]. In our microinvasive LCIS patients, three were small cell type and three others had large cells mixed with small cells. A close association of ductal extension of LCIS and microinvasion may be significant.

Tulusan's report describing the disruption of the basement membrane that is associated with the process of invasion, appears relevant [9]. Among four mastectomy patients, one was performed as a prophylactic procedure incidental to mastectomy for invasive lobular carcinoma present in the opposite breast. Three other women elected mastectomy. One patient underwent lumpectomy and axillary dissection and another patient, who was 84 years old, had a lumpectomy. No one had nodal metastasis and

no disease recurred in these patients during the short period of observation to date.

The current understanding on LCIS is that it is a marker of high risk. Some prefer to call it "lobular neoplasia" [10,11]. Based on the six patients described in this report, this assumption may not be correct. At least in some patients with LCIS, the progression to microinvasive lobular carcinoma does take place; that is, it is a pre-invasive carcinoma. In this context, Foote and Stewart [1] may have named this disease correctly; "lobular carcinoma in situ."

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